

## REMARKS

### **Status of the claims**

Claims 1, 3, 4, 6-9, 12-21 and 23-34 were pending in this application. Claim 23 has been amended. No claims have been canceled nor added. Upon entry of these amendments, claims 1, 3, 4, 6-9, 12-21 and 23-34 will remain pending and under active consideration. Claims 1, 16, and 21-23 are independent.

Applicants respectfully request entry of the amendments and remarks made herein into the file history of the present invention. Reconsideration and withdrawal of the rejections set forth in the above-identified Office Action are respectfully requested.

### **Claim amendments**

Claim 23 has been amended to provide a nexus between the recited steps (a)-(b) and the preamble. Applicants submit respectfully that the amendment presented herein is supported fully by the claims and/or specification as originally filed and, thus, does not represent new subject matter.

### **Response to Amendment**

Applicants sincerely thank the Examiner for withdrawing the new matter rejection (35 U.S.C. §112, first paragraph) in light of Applicants' submission dated October 17, 2005. Applicants further thank the Examiner for apparently withdrawing the rejection under 35 U.S.C. § 102(b) for want to novelty over Reid *et al.*

### **Claim rejections under 35 U.S.C. §112, second paragraph**

Claims 23-34 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to point out particularly and claim distinctly the subject matter regarded as the invention for the reasons of record. In particular, the Office Action alleges that "there is no nexus between the recited steps (a)-(b) and the preamble reciting 'processing a liver tissue.'" This

is because both the harvesting and processing steps do not even require a liver tissue as claimed.” Emphasis in original. Applicants traverse respectfully.

Without acquiescing in the propriety of rejection, and solely to advance prosecution of the present application, claim 23 has been amended to recite, in part, the step of “providing a donor having a non-beating heart between about 2 hours and 30 hours postmortem.” On this basis, Applicants suggest respectfully that the rejection has been overcome, and Applicants request respectfully that the 35 U.S.C. § 112, second paragraph, rejection be withdrawn.

### **Claim rejections under 35 U.S.C. § 103**

Claims 1, 3-4, 6-9, 12-21 and 23-34 stand rejected as allegedly being unpatentable over by PCT Application No. WO 95/13697 to Reid *et al.* (hereinafter, “Reid”) in view of U.S. Patent No. 6,129,911 to Faris (hereinafter, “Faris”) and PCT Application no. WO 91/07086 to Brockbank *et al.* (hereinafter, “Brockbank”) for the reasons of records. Applicants traverse this rejection and discuss each basis for rejection below.

#### All of the elements of the claimed invention are not taught.

In order to establish a prima facie case of obviousness, the Examiner is no doubt aware that the cited reference(s) must teach or imply *all* the elements claimed in the invention. As for the primary reference, Examiner concedes, and Applicants concur, that “Reid et al. do not specifically teach a method of processing a non-fetal donor liver tissue or procuring liver progenitor cells from a liver tissue obtained between about 2 hours and about 30 hours postmortem.” Emphasis by the Examiner. Neither Faris nor Brockbank cure this deficiency.

While Faris does disclose at column 5, lines 6-7, that tissue may be obtained from a deceased donor or an aborted fetus, the method for isolating progenitors actually disclosed by Faris, at column 6, lines 5-23, provides that the isolation process begins *immediately following anesthetization* of the donor, *i.e.*, while the donor is still alive with a beating heart. And, in any event, like Reid, Faris is silent with respect to processing a non-fetal donor liver tissue or

procuring liver progenitor cells from a liver tissue obtained between *about 2 hours and about 30 hours postmortem*.

Applicants kindly remind the Examiner the importance to consider any reference “as a whole,” and not piece-meal. Anything less and Applicants respectfully submit that the Examiner is liable to use impermissible hindsight in an attempt to arrive at the invention as presently claimed. “It is insufficient to select from the prior art the separate components of the inventor’s combination, using the blueprint supplied by the inventor.” *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 1143, 227 USPQ2d 543, 551 (Fed. Cir. 1985).

Brockbank does not materially add to the teachings of Reid nor Faris as discussed above. In the “background information” cited by the Examiner, Brockbank merely states what was accepted in the art at the time of the present invention, namely, that ischemia “ensues rapidly upon death of an organism.” With respect to kidneys, Brockbank states that these organs must be procured “immediately” after cessation of donor heartbeat. Bone marrow, Brockbank states, may “tolerate at least 12 hours of warm ischemia post mortem.” In fact, Brockbank is silent with respect to *liver* tissue viability, let alone viability “about 2 hours and about 30 hours postmortem.”

Simply put, the cited references, alone or in combination, fail to teach, at least, the element of processing a non-fetal donor liver tissue or procuring liver progenitor cells from a liver tissue obtained between *about 2 hours and about 30 hours postmortem*. This fact, alone, undermines a *prima facie* case of obviousness.

There exists no reasonable expectation of success.

Assuming *arguendo* that the elements of the current invention could be found in some combination of the referenced documents, there exists no reasonable expectation of success in combining or modifying same. The Office Action rests its entire case for expectation of success on the following one sentence: “An ordinary skilled artisan would have a reasonable expectation of success to carry out the above modification in light of the teachings of [the cited references], coupled with a high level of skills of an ordinary skilled artisan in the relevant art.” This is a

conclusion, and no support for this allegation can be found in the Office Action. Applicants respectfully traverse this position.

At the outset, Applicants kindly note that the standard for obviousness is based on one *ordinarily* skill in the art, not on one with “high level” of skills. In any event, Reid, Faris and Brockbank all suggest one notion, which was the dominant thought in the art, *i.e.*, that processing a non-fetal donor liver tissue or procuring liver progenitor cells from a liver tissue must take place “immediately” upon death. This conclusion is further supported by data collected by the Scientific Registry of Transplant Recipients (“SRTR”). The table below, which has been previously presented in prosecution, is worth reiterating here:

Warm Ischemic Time (minutes) after Cardiac Death of Liver Donors in the United States											
Year	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003
N	9	10	8	12	17	24	23	39	70	79	113
Mean	67	60	60	50	51	51	51	41	38	37	35
Minimum	46	30	38	30	1	19	1	1	1	0	1
Maximum	110	84	83	60	95	99	78	87	99	85	126

The table starkly shows that for a span of *nine* years, leading up to and including the filing date of the instant application (*i.e.*, 2001), **not a single** liver was transplanted from donors with a warm ischemic time of greater than about 2 hours. In fact, of the 404 liver transplants during the 11 year time span tabulated above, entirely 403 of them were with livers explanted *within* 2 hours of death. Put simply, one skilled in the art, being aware of this data, could only reasonably conclude that tissue greater than about 2 hours postmortem is unsuitable for transplantation.

At best, therefore, the cited references and the state of the art at the time of the instant invention teach “away” from the instant invention. Hence, none of the references can reasonably be relied upon to support a case of “reasonable expectation of success.”

There exists no motivation to combine the reference teachings.

Assuming *arguendo* that all of the individual elements of the pending invention are provided in the cited references and second, that *arguendo*, there exists a reasonable expectation of success in combining the teachings of the references, it is nonetheless difficult to argue that there is motivation for combining and/or modifying the teachings. The Examiner's allegation that one of ordinary skill in the art would have been motivated to modify the reference teachings also rests entirely in a single-sentence conclusion: "liver tissue from deceased donors and cadavers, particularly from humans, in any time frame between 2 hours and about 30 hours postmortem are available for obtaining an enriched population of liver stem and/or progenitor cells."

The Examiner's allegation however cannot be sustained. First, the *prior art* must suggest the desirability of the claimed invention. *See* subject heading, MPEP § 2143.01. Here, the Examiner has found motivation in the *Applicant's* disclosure. Second, the Examiner has taken the invention itself as cause for motivation. As noted above, however, there simply is no teaching or even suggestion that non-fetal donor liver tissue may be processed or liver progenitor cells procured from liver tissue obtained between about 2 hours and about 30 hours postmortem. Accordingly, Applicants respectfully submit that the Examiner's basis for "motivation" is simply impermissible.

Accordingly, Applicants submit respectfully that the rejection of claims 1, 3, 4, 6-9, 12-21 and 23-34 under 35 U.S.C. § 103 has been traversed, and Applicants request respectfully that the rejection of same claims be withdrawn.

#### **Request for personal interview**

In accordance with rules of practice set forth in the M.P.E.P. § 713.01, undersigned counsel(s) for Applicants hereby request the courtesy of a personal interview with the Examiner at a time and date of the Examiner's convenience. Applicants' counsel may be reached in our Washington, D.C. office by telephone at (202) 295-4621. Applicant believes that the present

application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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By 

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